UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/026,963 | 12/27/2001 | Mark D. Velligan | 033052-007 | 7363 |

7590 11/03/2003

Gerald F. Swiss, Esq.
BURNS, DOANE, SWECKER & MATHIS, L.L.P.
P.O. Box 1404
Alexandria, VA 22313-1404

| EXAMINER | |
|---|---|
| WRIGHT, SONYA N | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1626 | |

DATE MAILED: 11/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/026,963 | VELLIGAN ET AL. | |
| | Examin r | Art Unit | |
| | Sonya Wright | 1626 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --*

**Peri d for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-22 is/are pending in the application.

4a) Of the above claim(s) 17-19 and 22 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 15 and 16 is/are rejected.

7)☒ Claim(s) 1-16,20, and 21 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

This action is in response to Applicant's response filed 7-31-03. Claims 1-22 are pending in this application. Claims 17-19 and 22 are withdrawn from consideration. The objection to claims containing non-elected subject matter has been maintained. The rejection of claims 15 and 16 under 35 U.S.C. 112 is maintained. The objection to the abstract is overcome with Applicant's amendment.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 15 is rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the treatment of any disease caused by pathogenic organisms wherein said organisms are selected from the group consisting of bacteria, fungi, and parasites. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,

2. the state of the prior art,

3. the predictability or lack thereof in the art,

4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of the skill in the art.

*The Nature of the Invention*

The invention provides polyamide compounds that are useful in the treatment of diseases caused by pathogenic organisms. The compounds of the present invention are also useful in the treatment of cancer. Claim 15 is drawn to the treatment diseases caused by pathogenic organisms wherein said organisms are selected from the group consisting of bacteria, fungi, and parasites, with the instant compound.

*The State of the Prior Art*

Applicant states that the binding of the antibacterial netropsin and distamycin to AT-rich sequences in the minor groove of double stranded DNA is a well studied phenomenon. Further, Applicant states that because such binding can be used to regulate DNA expression, e.g. by blocking and/or displacement of regulatory proteins, or by inhibiting the activity of enzymes acting on DNA, such as reverse transcriptase or topoisomerase, optimization of this binding has been the subject of numerous recent studies. Applicant states that it would be desirable to provide compounds which reduce monodentate binding but which provide suitable geometries for bidentate binding and thus assist in combating diseases such as cancer and those caused by pathogenic agents such as bacteria and fungi.

*The predictability or lack thereof in the art*

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable because of the large number of diseases caused by pathogenic organisms wherein said organisms are selected from the group consisting of bacteria, fungi, and parasites. The various diseases caused by pathogenic organisms wherein said organisms are selected from the group consisting of bacteria, fungi, and parasites have different causative agents, and consequently, differ in treatment protocol.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

*The amount of direction or guidance present*

On page 1, lines 16-18, Applicant states that the compounds of the present invention are useful in the treatment of diseases caused by pathogenic organisms such as viruses, bacteria, parasites, and fungi and cancer. On pages 41-44, Applicant gives

guidance on utility, testing, and administration. On pages 80-82, Applicant gives guidance on the preparation of several formulations. The only disease that Applicant identifies as being treatable by the instant invention is cancer, see page 1, lines 18-19. However, a claim drawn to the treatment of diseases caused by pathogenic organisms such as viruses, bacteria, parasites, and fungi, embraces a large number of diseases.

*The presence or absence of working examples*

Applicant lists biological examples on pages 82-93. In the biological examples, a toxicity screen was done on a WST-CEM T-cell line and the minimum percent verses a no drug control was measured. Topoisomerase inhibition assays were performed, DNA binding properties of the instant compounds were studied, and anti-tumor assays were performed. Applicant provides Tables 1 and 2, wherein compounds of the invention were tested in assays and found to be active. The limited examples do not embrace the full scope of the claim.

*The breadth of the claims*

The breadth of the claims is that the instant compound can treat any disease caused by pathogenic organisms wherein said organisms are selected from the group consisting of bacteria, fungi, and parasites.

*The quantity of experimentation needed*

Undue experimentation is needed to use the instant invention. One of skill in the art would need to determine what diseases are caused by the pathogenic organisms bacteria, fungi, and parasites, and one would further have to determine whether the claimed compounds would provide treatment for said diseases.

*The level of the skill in the art*

The level of skill in the art is high. Due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the instant compound for the treatment of diseases caused by pathogenic organisms wherein said organisms are selected from the group consisting of bacteria, fungi, and parasites. As a result, one of ordinary skill in the art would need to perform an exhaustive search for which diseases caused by the pathogenic organisms bacteria, fungi, and parasites can be treated by the instant compound in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that "a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases caused by the pathogenic

organisms bacteria, fungi, and parasites can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome by Applicant listing in claim 15 the diseases caused by the pathogenic organisms bacteria, fungi, and parasites that can be treated by the instant invention. Any diseases listed in the claim should be supported in the specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 is drawn to "a method for the treatment of diseases caused by pathogenic organisms". It appears that Applicant intends for claim 16 to be further limiting of claim 15 by reciting in claim 16 that "the disease is cancer". However, in the specification, on page 1, lines 16-19, and on page 2, lines 23-26, "cancer" is not listed as a disease caused by a pathogenic organism. Appropriate correction is required.

***Claim Objections***

Claims 1-16, 20 and 21 are objected to as containing non-elected subject matter. This objection may be overcome by limiting the claims to the elected subject matter identified in the previous Office Action. As a result of the election and the corresponding scope of the invention identified for examination, the remaining subject matter of claims 1-16, 20, and 21 is withdrawn from further consideration pursuant to 37

CFR 1.142 (b) as being drawn to non-elected inventions. The withdrawn compounds contain varying functional groups such as the heteroaryl compounds: piperazino, quinolinyl, pyrimidinyl, benzimidazolyl, etc. which are chemically recognized to differ in structure and function. This recognized chemical diversity of the functional groups can be seen by the various classification of these functional groups in the U.S. classification system, i.e. class 544, piperizino and pyrimidinyl; class 546, quinolinyl; and class 548 benzimidazolyl; etc. . . Therefore the subject matter which is withdrawn from consideration as being non-elected subject matter differs materially in structure and composition and has been restricted properly. A reference which anticipated the elected subject matter would not even render obvious the withdrawn subject matter and the fields of search are not co-extensive.

***Response to Arguments***

Applicant's arguments filed 7-31-03 have been fully considered but they are not persuasive. Regarding the restriction requirement, Applicant argues that in recasting claim 1 as per the Office Action, the Examiner has divided Applicants' claim 1 into different alternative Markush Groups. Applicant further argues that such recasting of a claim is improper because it is inconsistent with the applicable case law and with the Patent Office's stated guidelines for treatment of Markush groups as set forth in MPEP § 803.02.

However, it is pointed out that the restriction requirement is made under 35 U.S.C. 121. 35 U.S.C. 121 gives the Commissioner (Director) the authority to limit the examination of an application where two or more independent and distinct inventions

are claimed to only one invention. The Examiner has indicated that more than one independent and distinct invention is claimed in this application and has restricted (limited) the claimed subject matter accordingly. Thus, the requirement to restrict the claims in this application is predicated on the fact that the claimed subject matter involves more than one independent and distinct invention. No where to Applicants argue to the contrary. No where do Applicants point out and give reasons why the claims do not involve independent or distinct subject matter. Accordingly, the restriction is proper. Moreover, it would constitute a burden to extend the search because separate search considerations would be involved in both the U.S. Patents and in the literature. The examination process following the search could easily result in different and thus burdensome considerations.

The restriction requirement here is predicated on the premise that the various compounds involved differ in structure and element so much so as to be patentably distinct, i.e. a reference which anticipated the elected compounds claimed would not even render obvious the others. Again, 35 U.S.C. 121 gives the Commissioner the authority to limit the examination of an application to a single invention. Applicant has not presented evidence that the examined subject matter is patentably indistinct from the non-examined subject matter. Moreover, the number of variables, their huge possibilities, and the various permutations and combinations thereof result in compounds so numerous and diverse so as to be a burden to classify, search, and examine. Accordingly, the requirement to restrict is considered proper and is

maintained. The search and examination of the application is directed to the generic embodiment identified for examination only.

Regarding the rejection of claim 15 under 35 U.S.C. 112 first paragraph, Applicant's amendment specifies pathogenic organisms which cause diseases: bacteria, fungi, and parasites, however, Applicant does not provide a listing of said diseases. There are a large number of diseases caused by bacteria, fungi, and parasites. Applicant does not show support that the instant compound can treat all of said diseases. Therefore, a lack of enablement exitsts in claim 15. See the rejection under 35 U.S.C. 112 first paragraph, supra.

Regarding the rejection of claim 16 under 35 U.S.C. 112 second paragraph, Applicant has not amended claim 16, or presented arguments in response to the rejection of claim 16, therefore the rejection is maintained.

The objection to the abstract has been overcome with Applicant's amendment.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sonya Wright, whose telephone number is (703) 308-4539. The examiner can normally be reached on Monday-Friday from 8:00 AM - 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane, can be reached at (703) 308-4537. The Unofficial fax phone number for this Group is (703) 308-7922. The Official fax phone numbers for this Group are (703) 308-4556 or 305-3592.

When filing a FAX in Technology Center 1600, please indicate in the Header (upper right) "Official" for papers that are to be entered into the file, and "Unofficial" for draft documents and other communications with the PTO that are not for entry into the file of the application. This will expedite processing of your papers.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [joseph.mckane@uspto.gov]. All Internet e-mail communications will be made of record in the application file. PTO employees will not communicate with applicant via Internet e-mail where sensitive data will be exchanged or where there exists a possibility that sensitive data could be identified unless there is of record an express waiver of the confidentiality requirements under 35 U.S.C. 122 by

the applicant. See the Interim Internet Usage Policy published by the Patent and Trademark Office Official Gazette on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-1235.

Joseph K. McKane

Supervisory Patent Examiner

Group 1600

Sonya Wright

October 23, 2003